The Solvolysis of Crotyl Chloride in 90% Aqueous Ethanol.—A mixture of 75 g. (0.83 mole) of crotyl chloride, 200 ml. of absolute ethanol, 20 ml. of water, and 95 g. of calcium carbonate was stirred and refluxed on an oil-bath (85°) for one hundred hours. The calcium carbonate was filtered out and washed with 50 ml. of ethanol, and the washings were added to the filtrate. The alcoholic solution of the product was added to 1.5 liters of water. The mixture was extracted with a total of 400 ml. of carbon disulfide and dried briefly over potassium carbonate. Fractionation of this material was carried out on the three foot Podbielniak type column. Fractions containing other than carbon disulfide, alcohol and water were

Fr. 1	1.9 g.	48.0–76.0° (uncor.)	n^{20}D 1.5030
Fr. 2	2.0 g.	76.0–98.6°	n^{20}D 1.4010
Fr. 3	24.9 g.	98.6–99.0°	n^{20}D 1.4049 (crotyl ethyl ether)

It was estimated that not more than 1.2 g. of methylvinylcarbinyl ethyl ether (b. p. 77.6°, n^{21}D 1.3751)[2a] out of a total of 27.6 g. of ether was formed in this reaction. The yield of ether was 33%.

Summary

The hydrolysis of crotyl and methylvinylcarbinyl chlorides has been studied using a variety of experimental conditions designed to produce different ratios of S_N1 and S_N2 replacement reactions, and the compositions of butenols from these reactions have been determined. The secondary chloride appears to react only by the S_N1 type process to give a mixture of allylic isomers while the primary chloride responds readily to changes in experimental conditions, giving relatively larger amounts of normal product as the medium becomes more suitable for a bimolecular reaction.

Kinetic studies of the reaction of the isomeric chlorides in dilute solutions of sodium hydroxide in aqueous ethanol showed that the secondary chloride reaction rate was independent of hydroxide ion; the primary chloride, however, showed both first and second order kinetics. Evidence was obtained that the first order reaction of the primary chloride is in part a bimolecular reaction with solvent.

LOS ANGELES, CALIFORNIA RECEIVED SEPTEMBER 7, 1943

[CONTRIBUTION FROM THE NUTRITIONAL RESEARCH DEPARTMENT, ABBOTT LABORATORIES]

The Hydrolysis of Pantothenate: A First Order Reaction.[1] Relation to Thiamin Stability

BY DOUGLAS V. FROST AND FLOYD C. MCINTIRE

A rapid polarimetric method for following the hydrolytic decomposition of pantothenate in aqueous solution was described recently in a paper from this Laboratory.[2] Reaction rate analyses applied to the data of this earlier publication clearly show that at the temperature studied, 60°, pantothenate hydrolysis follows the pattern of a first order reaction with respect to pantothenate concentration. The effect of varying *p*H at that temperature demonstrates that pantothenate stability is good in the *p*H range 5.5–7, but that hydrolysis proceeds at an increasing rate with increase in acidity below *p*H 5.5. The present study deals with the temperature variation of the rate of pantothenate destruction at constant *p*H.

Procedure.—A *p*H of 3.7–4.0 was chosen since the formation of pantoyl lactone is rapid and complete in this range.[2] The specific rotation of 1% calcium pantothenate at *p*H 3.8 was found to be +24.2°. A standard reference curve was therefore plotted from −27.5 to +24.2° and estimations of residual pantothenate were made as previously described.[2]

Two solutions of 1% calcium pantothenate, one buffered with 3% monosodium phosphate, the other unbuffered, were studied in parallel. Addition of small amounts of concentrated hydrochloric acid was required at the start and from time to time during the experiments to maintain a *p*H of 3.8 as closely as possible. Since the necessary additions of acid were small, no corrections were made for dilution. The various temperatures of reaction were maintained constant within 0.5°. Samples were withdrawn from the reaction vessels to make the rotation measurements.

The results obtained are shown in Table I.

Discussion.—When the logarithm of the concentration of pantothenate was plotted against time, straight lines, characteristic of a first order reaction, were obtained at each of the temperatures studied. The values of *k* in Table I have therefore been calculated using the standard first order equation.

The rate of destruction of pantothenate was slightly greater in the buffered solutions than in the unbuffered ones. The effect of phosphate buffer, as well as other substances, in catalyzing pantothenate destruction is more pronounced at higher *p*H,[2] than at the relative low *p*H of this study. The values for the unbuffered and buffered solutions in this case are close enough to serve as a partial check against one another.

In Table II the average values for *k* at different temperatures are shown, together with a calculation of the half-life period for each. When the values for log *k* are plotted against $1/T$, the results are seen to follow the Arrhenius equation in yielding a straight line, as shown in Fig. 1. From the slope of this line an activation energy of 19,000 ± 1000 cal. may be calculated. By extrapolation of the data the value for the half-life at 0° is found to be 6030 days, while at 110 and 120° it is 0.174 and 0.096 day, respectively.

Studies also were made to determine whether

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[1] Reported in part before the American Chemical Society at Pittsburgh, Pa., September 9, 1943.

[2] D. V. Frost, *Ind. Eng. Chem.*, *Anal. Ed.*, **15**, 306 (1943).

TABLE I

TEMPERATURE VARIATION OF RATE OF DESTRUCTION OF PANTOTHENATE

Original solutions at each temperature contained 1% calcium pantothenate, $Ca(Pa)_2$, corresponding to 21 millimoles per liter. Solutions had $\alpha^{25}D$ of +24°, *p*H of 3.7–4.

		Buffered[a]			Unbuffered		
Temp., °C.	Time, days	$\alpha^{25}D$	Concn. $Ca(Pa)_2$, millimoles per liter	k,[b] days^{-1}	$\alpha^{25}D$	Concn. $Ca(Pa)_2$, millimoles per liter	k,[b] days^{-1}
100	0.083	+16	17.75	2.38	+15.7	17.5	2.18
100	0.25	+ 3	12.2	2.17	+ 4.5	13	1.92
75	6	−23	1.68	0.42	−22	2.1	0.384
55	9	− 5.5	8.8	.0965	− 3.5	9.65	.0864
55	15	−12	6.1	.0823	−10.5	6.71	.075
39	9	+18	18.5	.0143	+19.5	19.26	.0106
39	15	+13.5	16.5	.0159	+17.5	18.4	.0087
39	21	+12	16	.0125	+14	16.8	.0106
39	29	+ 8	14.3	.0133	+ 9	14.7	.0123
39	42	+ 2	11.9	.0135	+ 4	12.7	.0119
39	60	− 4	9.45	.0133	− 3	9.87	.0126
39	90	− 9	7.35	.0117	− 5	9.03	.0094
39	107	−15.5	5.5	.0125	−13.5	5.56	.0124
39	121	−17.5	3.88	.0134	−14	5.35	.0113
23	15	+21.7	20	.00325	+23.2	20.6	.001280
23	29	+19	18.9	.00359	+20	19.3	.00290
23	42	+17	18.1	.00352	+17.5	18.3	.00327
23	60	+15.5	17.4	.00311	+15	17.2	.00332
23	90	+14	16.8	.00248	+14	16.8	.00248
23	121	+10.5	15.3	.00267	+10.5	15.3	.00261
10	42	+22.5	20.4	.000704	+24	21	.....
10	60	+22.2	20.2	.000654	+23	20.5	.000401
10	107	+22	20	.000455	+22	20.0	.000455
10	121	+22	20	.000402	+22	20.0	.000402

[a] Buffered solutions contained 3% monosodium phosphate. [b] Constants calculated by formula $K = 2.303/t \log C_0/C$.

the rate of pantothenate destruction at *p*H 3.7–4 depended on the buffer used. Buffers tried were 3 and 6% glycine, 3 and 6% β-alanine, 2 and 5% nicotinamide and 3% acetic acid. In all cases the amounts of destruction at 39° over a period of ninety days were about equal. Thus the rate of destruction in this acid range appears to be independent of the type of buffer.

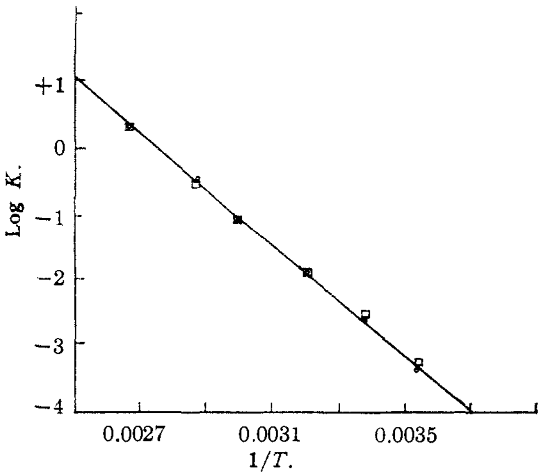

Fig. 1.—The temperature variation of the rate of hydrolysis of pantothenate: O, rate of hydrolysis unbuffered; □, rate of hydrolysis buffered with 3% monosodium phosphate.

TABLE II

SUMMARY OF VELOCITY CONSTANTS AT VARIOUS TEMPERATURES IN DECOMPOSITION OF PANTOTHENATE

	Buffered		Unbuffered	
Temp., °C.	k, ave.	half-life, days	k, ave.	half-life days
100	2.28	0.304	2.05	0.338
75	0.42	1.7	0.384	1.8
55	.0894	7.8	.0811	8.5
39	.0137	50.6	.0111	62.4
23	.00310	224	.0027	257
10	.000554	1250	.00042	1650

Relative Stability of Pantothenate and Thiamin.—A solution of 0.1% thiamin hydrochloride in 3% monosodium phosphate was divided into several equal parts. The separate parts were adjusted to various *p*H values by the addition of small amounts of hydrochloric acid or sodium hydroxide. A 1% solution of calcium pantothenate was treated in like manner. The separate solutions were filtered, sealed in ampoules and immediately placed in an autoclave for fifteen minutes at 15 lb. pressure. The amounts of thiamin and pantothenate remaining after removal from the autoclave were determined by the thiochrome and rotation methods, respectively.

Figure 2 shows the percentage of original pantothenate and thiamin remaining at each pH studied. The maximum shift in pH during autoclaving was 0.2 unit. The point at which the two curves cross, pH 4.6, represents the condition under which destruction of the two compounds is equally rapid. In other experiments using somewhat different conditions some variation in the slope of the curves and in the point at which they cross has been noted. In general, however, the latter point falls in the pH range 4.5–4.8.

That stability of thiamin is favored by acid conditions has been known for some time.[3,4] More recently the thermal decomposition of thiamin was shown to be a first order reaction at a number of different acidities.[5] Reports have since appeared that the type of buffer used has a large effect on the rate of this decomposition at different acidities.[6,7]

In contrast to this, stability of pantothenate has been shown to be largely independent of the presence or type of buffer at pH 3.7–4. Other studies, however, have confirmed the earlier indications that buffer substances cause significant increases in the rate of destruction in the pH range 4–7. The positive effect of nicotinamide or phosphate in hydrolysis of pantothenate is most apparent in the range in which pantothenate is normally most stable, *i. e.*, pH 5–7.

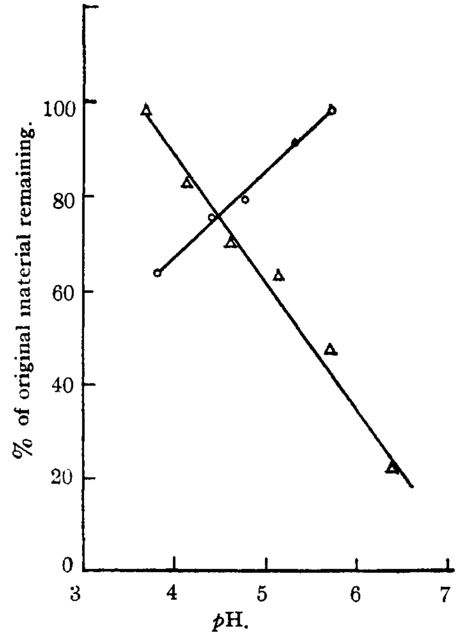

Fig. 2.—Relative rates of destruction of calcium pantothenate and thiamin hydrochloride in acid solution: O, 1% solution of calcium pantothenate; △, 0.1% solution of thiamin hydrochloride. All solutions were run in an autoclave at 15 lb. pressure for fifteen minutes.

Destruction of thiamine appears from the facts at hand to be considerably more complicated than that of pantothenate. Rate of hydrolysis of pantothenate is chiefly a function of pH, but may be catalyzed by the presence of electrolytes. Destruction of thiamin, however, appears to be subject to many influences other than pH and may even be inhibited by presence of certain compounds.

Summary

Hydrolysis of pantothenate in acid solution follows a first order relation with respect to pantothenate concentration.

The activation energy of the reaction has been measured to be 19,000 cal., corresponding to an increment per 10° of 2.6.

The contrasting effect of acidity on rate of hydrolysis of thiamin and pantothenate has been studied and discussed.

NO. CHICAGO, ILLINOIS RECEIVED NOVEMBER 8, 1943

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[4] B. C. Guha and J. C. Drummond, *Biochem. J.*, **23**, 880 (1929).

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[6] B. W. Beadle, D. A. Greenwood and H. R. Kraybill, *J. Biol. Chem.*, **149**, 339 (1943).

[7] F. C. McIntire and D. V. Frost, Abstracts 106th meeting Amer. Chem. Soc., Pittsburgh, Sept. 1943, p. 63.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Solubility of Aluminum Bromide in n-Butane

BY JULIUS D. HELDMAN[1] AND CARL D. THURMOND

Aluminum bromide exists as the dimer in the crystal, in the molten salt, in solution in non-basic solvents, and in the vapor phase over a wide range of conditions. Although it forms highly polar double salts and complexes with organic bases, it would be expected to show normal solubility characteristics in non-polar, inert solvents, of which the paraffin hydrocarbons are good examples.

It has been shown that pure, dry aluminum bromide exerts no catalytic influence on the butanes[2] or n-heptane,[3] even though in the presence of a "promoter" (a hydrogen halide or substance capable of producing hydrogen bromide by reaction with the salt) aluminum bromide acts as a catalyst for paraffin conversions, notably isomerization.[2,3,4]

The stability of n-butane in dry aluminum

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[1] National Research Fellow in Chemistry, 1942-1943.

[2] Leighton and Heldman, THIS JOURNAL, **65**, 2276 (1943).

[3] Sensel, Dissertation, Western Reserve University, Cleveland, Ohio, 1938.

[4] See Egloff, Hulla and Komarewsky, "Isomerization of Pure Hydrocarbons," Reinhold Publishing Corporation, New York, N. Y., 1942, Chapter 1 and Tables, pp. 218, *et seq.*